to the claims. The specification has also been amended to address certain formalities. Applicants submit that these amendments raise no issue of new matter. Thus, claims 81-91 are now pending and under examination.

Pursuant to the requirements of 37 C.F.R. 1.121, applicants annex hereto as **Exhibit A** a copy of the amended paragraph of the specification marked up to show the changes made herein relative to the previous version thereof.

In view of the arguments set forth below, applicants maintain that the Examiner's rejections made in the October 10, 2001 Final Office Action have been overcome, and respectfully request that the Examiner reconsider and withdraw same.

Drawings

The drawings have been objected to by the Draftsperson under 37 C.F.R. 1.84 or 1.152.

In response, applicants will submit corrected Figures at such time as the instant claims are deemed allowable.

Information Disclosure Statement

The Examiner stated that a listing of references in the specification, such as that which appears on pages 87-100 of the instant specification, is not a proper Information Disclosure Statement, and therefore the listed references will not be considered.

In response, applicants note that they submitted an Information Disclosure Statement on November 9, 2000, containing the references deemed most pertinent to the present invention. Applicants further note that the listing of references in the application was never intended to serve as an Information Disclosure Statement.

Oath/Declaration

The Examiner noted that a new oath or declaration is required in order to correct an error in the listing of the filing date for the priority document, U.S. Serial No. 09/017,976.

In response, applicants respectfully request that the Examiner enter **Exhibit B** of applicants' April 10, 2002 Amendment, a revised Declaration and Power of Attorney which lists the corrected filing date of U.S. Serial No. 09/017,976 as February 3, 1998.

Specification

The Examiner notes that references to trademarks in the specification should be capitalized.

In response, applicants will submit a corrected version of the paragraphs containing references to trademarks in due course.

Rejection Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 71-74, corresponding to new claims 83-86, under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Examiner stated that the specification lacks complete deposit information for the deposit of the hybridoma cell lines and monoclonal antibodies B152, B207, B108 and B109. The Examiner also indicated that amending the specification to conform with the current practice regarding restrictions to public access to hybridoma cell lines would obviate the rejection.

In response, applicants have amended the specification to conform with current practice regarding restrictions to public access to the hybridoma cell lines producing the B152, B207, B108 and B109 antibodies.

In view of the above remarks, applicants maintain that new claims 83-86 satisfy the requirements of 35 U.S.C. §112, first paragraph.

Provisional Obviousness-Type Double Patenting Rejection

The Examiner provisionally rejected claims 67-76 and 78-80, as allegedly unpatentable over claims 53-81 of copending application U.S. Serial No. 09/017,976 under the judicially created doctrine of obviousness-type double patenting. The Examiner stated that the preambles of the claims in the two applications, although reciting different purposes for the claimed method, nevertheless encompass the same subject matter and therefore are not given patentable weight.

In response to the Examiner's rejection of claims 69 and 70, but without conceding the correctness thereof, applicants note that these claims have been canceled, rendering the rejection thereof moot.

In response to the Examiner's rejection of canceled claims 67, 68, 71-76 and 78-80, corresponding to new claims 82, 81, and 83-91, applicants respectfully maintain their traversal for the reasons set forth in their July 17, 2001 Amendment and for the additional reasons set forth below.

U.S. Serial No. 09/017,976 is directed to methods for predicting the outcome of a pregnancy based on a determination of an early pregnancy-associated form of hCG (EP-hCG) in a urine sample. That invention is based upon both the discovery of EP-hCG itself and of a correlation between urinary levels

of EP-hCG early in the first trimester of pregnancy and a viable pregnancy.

The present invention is based upon the surprising discovery of a correlation between high EP-hCG levels and trophoblastic malignancy. This unexpected discovery permits the measurement of urinary EP-hCG levels to be used to diagnose this malignancy.

In contrast to the Examiner's position, applicants point out that the bodies of new claims 81-91, and not just their preambles, are clearly directed to methods for detecting trophoblast malignancy. Thus, applicants maintain that the instant claims are drawn to subject matter distinct from that claimed in U.S. Serial No. 09/017,976.

In view of these remarks, applicants maintain that new claims 81-91 are patentable over claims 53-81 of U.S. Serial No. 09/017,976.

Rejections Under 35 U.S.C. §103(a)

The Examiner rejected claims 67-70 and 72-80 under 35 U.S.C. §103(a) as allegedly unpatentable over Ellish et al (1996) and further in view of Birken et al (1993) and O'Connor et al, (1988).

In response to the Examiner's rejection of claims 69 and 70, but without conceding the correctness thereof, applicants note that these claims have been canceled, rendering the rejection thereof moot.

In response to the Examiner's rejection of canceled claims 67, 68, 72-76 and 78-80, corresponding to new claims 82, 81, and 84-91, respectively, applicants respectfully traverse.

The present invention is based upon the unexpected discovery that an early-pregnancy associated form of hCG, EP-hCG, correlates with trophoblastic malignancy. This discovery permits the measurement of urinary EP-hCG levels to be used in the diagnosis of trophoblastic disease.

Specifically, new claims 81-91 provide a method for detecting gestational trophoblast malignancy based upon a measurement of the amount of EP-hCG relative to that of intact hCG in the urine of a subject.

In asserting that the claimed methods are obvious over Ellish, Birken and O'Connor, the Examiner ignores applicants' unexpected discovery on which these methods are based and, in doing so, engages in hindsight.

Ellish teaches a two-site immunoradiometric assay used to quantitate hCG in urine samples in a prospective study of early pregnancy loss, wherein pregnancy was defined by the levels of hCG detected with the assay.

Birken teaches a method for the separation of intact hCG from nicked hCG and hCGβcf that may be useful in the production of improved reference standards for intact hCG.

O'Connor teaches an immunoradiometric assay to distinguish intact hCG from the free hCGβ subunit and fragments thereof.

For the reasons discussed above, applicants maintain that the combined teachings of Ellish, Birken and O'Connor do not suggest either the motivation for developing the instant methods or a reasonable expectation that such methods would succeed.

Regardless of whether the B108, B109 and B207 antibodies are disclosed in Ellish, Birken and O'Connor, the use of these antibodies to detect intact hCG does not suggest the methods

of the instant invention, which are based, in relevant part, on the discovery of a correlation between EP-hCG levels and trophoblastic malignancy. Thus, applicants maintain that the instant methods are not rendered obvious by the cited references when combined.

In view of the above remarks, applicants maintain that new claims 81, 82 and 84-91 satisfy the requirements of 35 U.S.C. §103.

Summary

In view of the amendments and remarks made herein, applicants maintain that the claims pending in this application are in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee, other than the enclosed $570.00 fee, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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